

# Pulmonary Aspergillosis Associated with COVID-19

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Received: 3rd May, 2021; Revised: 14th July, 2021; Accepted: 17th August, 2021; Available Online: 25th September, 2021

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## ABSTRACT

Among the potential pathogens in patients with COVID-19 that we should pay more attention to is Aspergillosis, as pulmonary Aspergillosis is a critical complication of patients with acute respiratory distress syndrome, especially those with severe pneumonia. In this study, *Aspergillus* sp. was isolated from patients with COVID-19 from the respiratory tract, and its presence was surveyed as a co-infection with a viral infection. The results showed that Aspergillosis constituted a relatively high percentage in patients 10.8% of the total infections, represented by four species (*Aspergillus tamaritii*, *Aspergillus flavus*, *Aspergillus candidus*, and *Aspergillus niger*). Also, the most susceptible age to infection with co-infections is the elderly, where the age of more than 60 years, and that diabetes is the most risk factor for infection with Aspergillosis accompanying the virus. Males were also more susceptible to co-infection than females.

**Keywords:** COVID-19, Pulmonary aspergillosis, Pneumonia, Respiratory distress syndrome.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.3.40

**How to cite this article:** Jasim NO, Klaaf M. Pulmonary Aspergillosis Associated with COVID-19. International Journal of Drug Delivery Technology. 2021;11(3):892-895.

**Source of support:** Nil.

**Conflict of interest:** None

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## INTRODUCTION

Since the first discovery of new pneumonia in Wuhan, China, the pathogen at the end of 2019, a severe acute respiratory syndrome coronavirus (SARS) has been discovered. The world has been working hard to understand and manage many issues, including preventing its spread, proper treatment, and vaccination. Co-infection between SARS-CoV-2 and other respiratory pathogens has become another serious concern in treating patients with COVID-19.<sup>1,2</sup> Among these potential pathogens in COVID-19 patients, we should pay more attention to Aspergillosis because invasive pulmonary Aspergillosis is challenging to diagnose and can be associated with higher mortality rates.<sup>3,4</sup> Therefore, testing for the presence of *Aspergillus* spp in lower respiratory secretions in COVID-19 patients in the ICU should be considered to allow timely treatment and avoid potential immunosuppression with medication. However, performing bronchoscopy in patients with COVID-19 is relatively contraindicated due to the biological risks and clinical deterioration caused by the procedure. Lung biopsy, which can also be considered a gold standard diagnostic method, is also impractical in such a case.<sup>5</sup> Studies and knowledge of the association of COVID-19 with pulmonary Aspergillosis are limited.<sup>6</sup> Therefore, we conducted this study that refers to the common pulmonary Aspergillosis in patients infected with COVID-19 to provide information on the subject that is still surrounded by a lot of ambiguity. The study deals with the isolation and

diagnosis of *Aspergillus* types from patients infected with the coronavirus and tabulates all the information about the patient that is useful in Knowing the risk factors for associated Aspergillosis.

## MATERIALS AND METHODS

### Collection of Specimens

Sputum samples were collected from patients using a container 5 cm in diameter. Samples were collected after rinsing the mouth with water to reduce oral bacteria and to dilute saliva. Sputum should not be placed in the mouth but should be spitting out immediately into a sterile container.<sup>7</sup>

### Cultivation of Specimens

Specimens taken from the patients were cultivated on the Sabouraud's dextrose agar by taking 0.1 mL of the sample and streaking on the surface of the medium. Then the dishes were incubated at 37°C for 48 hours, after which the results were recorded.<sup>8</sup>

### Identification of Fungal Isolates

According to the culture and microscopic characteristics mentioned in Koneman,<sup>9</sup> Howard,<sup>10</sup> the isolated fungi were diagnosed.

### Incidence of Disease

It is measured by the number of new events or disease states that develop in a group of at-risk individuals during a specified period of time.<sup>11</sup>

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$$Incidence\ rate\ (I) = \frac{Number\ of\ new\ cases\ of\ disease}{Population\ at\ risk}$$

**Information Form**

Information about the patients was collected according to the following form, which was used in the analysis of the results (Table 1).

**RESULTS AND DISCUSSION**

A total of 102 clinical specimens were taken from patients who tested positive for coronavirus (Covid-19) from Al-Diwaniyah General Hospital in Al-Diwaniyah city, Iraq from February 1 to April 1, and 11 samples showed positive for Aspergillosis while 91 are negative samples for Aspergillosis (Table 2).

Table 3 shows the percentage for the for Aspergillars that gave specimens with positive results, as it was 11 samples in percentage 10.8 % for Aspergillus associated with viral infections, which is a relatively high percentage compared to the rest of the infections, where the number of samples

for viral infections only was 20 samples, at a rate of 19.6%. At the same time, Viral infections with non-Aspergillus infection are 71 samples, with a rate of 69.6%.

Nasir,<sup>12</sup> reported that 147 patients had COVID-19 virus and Aspergillus species were isolated from tracheal sips of nine patients (39.1%), of these, five patients (21.7%) were diagnosed with COVID-19-associated Aspergillus and four (17.4%) have Aspergillus colonization. This ratio is close to what was found in our study. From Table 2, we calculated the incidence of Aspergillosis associated with COVID-19 as follows:

$$Incidence = \frac{Number\ of\ aspergillosis\ infections}{Total\ number\ of\ infections} \times 100$$

$$\frac{11}{104} \times 100\% = 10.8\%$$

Figure 1 shows the fungal species belonging to the genus Aspergillus that were isolated from patients infected with Aspergillus associated with viral infection, where four types of

**Table 1:** Information form

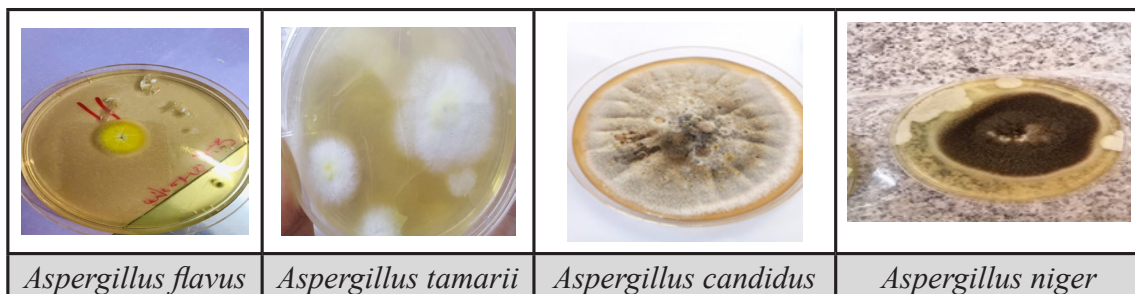
Character	Aspergillosis with covid- 19	Aspergillosis without covid -19	Total
Gender (male; female)			
Age			
Time			
admission in ICU			
Cancer			
Diabetes			
Chronic renal failure			
Liver disease			
Lung disease			
Hypotensive			
Surgery			
Cardiac disease			
Fever			
Receive treatment			
Species of fungal isolated			

**Table 2:** Clinical classification of patients

No. of patients	Positive Aspergillosis	Negative Aspergillosis	Total
102	11	91	102

**Table 3:** Infection analgesics

Type of infection	No .infection	Percentage %
COVID + Aspergillosis	11	10.8
COVID-19	20	19.6
COVID + other mycotic infection	71	69.6



**Figure 1:** Fungal species of Aspergillus isolated from patients infected with Aspergillus associated with viral infection.

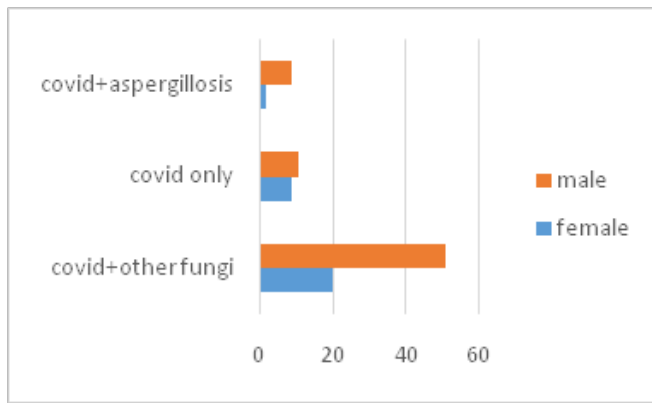


Figure 2: Distribution of infection according to the sex

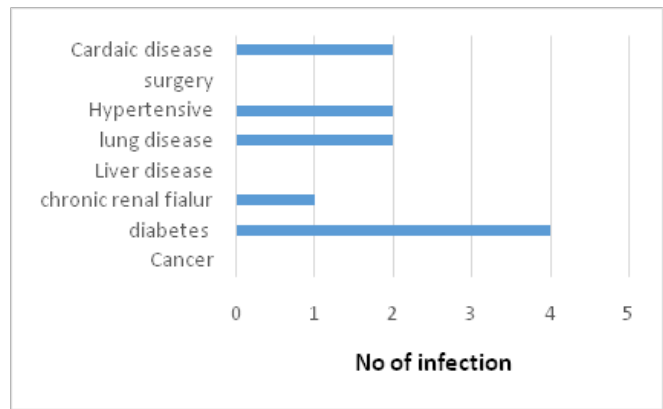


Figure 4: Distribution of infection according to chronic disease

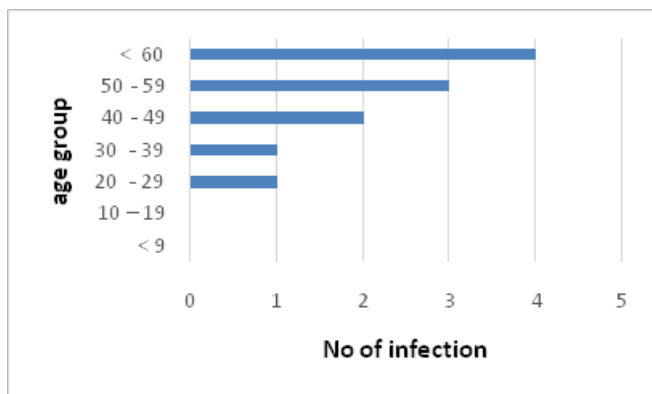


Figure 3: Distribution of infection according age group

Aspergillus were isolated, namely, *A. tamaritii* and *Aspergillus flavus*. *A. niger* *A. candidus*, while Falces<sup>13</sup> isolated *Aspergillus nidulans* and *Aspergillus fumigatus* from patients infected with *Aspergillus* associated with *Aspergillus* COVID-19. Also, in other study isolated *Aspergillus flavus* and *candida* from COVID-19 patients.<sup>14</sup>

Figure 2 shows the distribution of infections by sex. It is noted that the number of aspergillosis infections associated with COVID-19 is higher in males than females. This result may be because Estrogen has been demonstrated to modulate immunological response by decreasing negative selection of high-affinity auto-reactive B cells, modifying B cell function, and leading to Th2 response in general.<sup>15</sup>

Among the factors that were involved is the age factor and its effect on the distribution of fungal infections associated with the COVID-19 virus, as Figure 3 shows the distribution of the associated *Aspergillus* infection by age group. This is what was stated by Falces<sup>13</sup> that the average age of patients infected with *Aspergillus* associated with viral infection is 71 years.

When analyzing the data taken from patients and recorded in the information form, it was found that diabetes is a risk factor for infection with *Aspergillus* associated with COVID-19 (Figure 4).

These results agree with his findings Salmanton,<sup>14-16</sup> where showed that diabetes is one of the most chronic diseases affecting the incidence of *Aspergillus*. Patients with SARS-

CoV-2 have significant lung damage due to viral replication and the ensuing cytokine storm and complex inflammatory processes. Severe damage to lung tissue can lead to secondary infections within 17 days after onset of MERS-CoV disease. Immune competence who develop severe forms of COVID-19 with more than one underlying condition, such as COPD, hypertension, diabetes, or chronic kidney disease, and any of these predisposing factors are generally associated with an increased risk of developing fungal infections<sup>17-19</sup>

### CONCLUSION

Aspergillosis constitutes a serious health problem among patients infected with coronavirus (COVID-19), as it constituted (10.8%) of the total infections. Males had the highest rate of infection with aspergillosis associated infection with the virus. The most susceptible ages to infection with *Aspergillus* are the elderly. Also, Chronic diseases constitute a risk factor for infection with *Aspergillus* accompanying COVID-19, and diabetes constituted the most influential disease for infection with *Aspergillus* accompanying the virus. Accordingly, we recommend conducting more studies on fungi associated with coronavirus infections (COVID-19) and emphasizing the need for examination for fungal infections to diagnose early and allow appropriate antifungal treatment, and finally, given the rate of infection with *Aspergillus* accompanying COVID-19, which was reached in this study, which is considered relatively high for such infections, health institutions must give the matter importance and rehabilitate hospital laboratories to conduct fungal examinations for patients suspected of being infected with the virus.

### ACKNOWLEDGMENTS

Our thanks to the staff of the microbiology laboratory in the Al-Diwaniyah General Hospital

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